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Recommendations for Influenza and Other Respiratory Virus Testing and Reporting 2016–2017

The official start of the 2016–17 influenza season is October 2, 2016. This California Department of Public Health guidance for local health jurisdictions (LHJs) summarizes diagnostic testing guidelines and influenza reporting requirements for the 2016–2017 influenza season (October 2, 2016–September 30, 2017).

I. Highlights

- Continue mandatory reporting of laboratory-confirmed influenza fatal cases age 0–64 years by using CalREDIE or faxing the [Severe Influenza Case History Form](#) to **916-440-5984**.
- Continue voluntary reporting of laboratory-confirmed influenza cases age 0–64 years requiring intensive care by using CalREDIE or faxing the [Severe Influenza Case History Form](#) to **916-440-5984**.
- **NEW!!** Reporting of respiratory syncytial virus-associated deaths in children <5 years of age is now mandatory
- Please report these cases in CalREDIE and complete the [Respiratory Syncytial Virus Death Form](#) and either fax it to **916-440-5984** or upload it to the electronic filing cabinet in CalREDIE.
- Report acute respiratory outbreaks as soon as possible using CalREDIE or faxing the [Acute Respiratory Illness Outbreak Form](#) to **916-440-5984** in the following situations:
 - Outbreaks in institutions (e.g. long term care facilities, prisons, sleepover camps) with at least **one** case of laboratory confirmed influenza in the setting of a cluster (≥ 2 cases) of influenza-like illness (ILI) within a 72-hour period.
 - Associated with hospitalizations or fatalities.

- Assessed as having public health importance (e.g., case(s) have recent exposure to swine, recent travel to an area where novel influenza is circulating, or contact with a confirmed case of swine or novel influenza).
- Encourage influenza testing, preferably by real-time **RT-PCR**** (reverse transcription - polymerase chain reaction), for the situations listed below:
 - Hospitalized, intensive care unit (ICU) and/or fatal cases with ILI*
 - Acute respiratory outbreaks
 - ILI in any person where history of travel, or recent close contacts, or exposures within 10 days of symptom onset, suggests concern for variant or novel influenza infection (e.g., swine (H3N2v) influenza, influenza A/H7, influenza A/H5, or other novel influenza A). For additional information see:
 - <http://www.cdc.gov/flu/swineflu/variant.htm>
 - <http://www.cdc.gov/flu/avianflu/h7n9/case-definitions.htm>
 - <http://www.cdc.gov/flu/avianflu/h5n1/testing.htm>
 - http://www.cdph.ca.gov/HealthInfo/discond/Documents/CDPH_Influenza_H5N1_H7N9_HPAI_%20Quicksheet_final.pdf

**Influenza-like illness = fever ($\geq 100^{\circ}\text{F}$ or 37.8°C) and cough or sore throat, in the absence of a known cause other than influenza*

NOTE: Rapid influenza diagnostic tests (RIDTs) may vary in terms of sensitivity and specificity (ranging ~50–70%) when compared with RT-PCR. RIDTs may produce false positives, especially when influenza prevalence is low, and false negatives when influenza prevalence is high.

****Real-time RT-PCR** is the preferred laboratory testing method when there is strong clinical suspicion of influenza infection, even if the RIDT result is negative.

- Collect respiratory specimens for confirmatory testing and subtyping by real-time RT-PCR at a Respiratory Laboratory Network (RLN) public health laboratory or the CDPH Viral and Rickettsial Disease Laboratory (CDPH-VRDL).
- Work with community partners, e.g. hospital clinicians and clinical laboratories, to remind them of the importance of saving respiratory specimens so that follow-up subtyping can be performed by a public health laboratory.

II. **Diagnostic testing**

- Influenza real-time RT-PCR testing is available at CDPH-VRDL and at 27 RLN laboratories throughout the state. For consultations, please contact **VRDL Supervisor Hugo Guevara at 510-248-9855 or Hugo.Guevara@cdph.ca.gov**.
- Upper respiratory samples suitable for RT-PCR include: nasopharyngeal (NP) swabs, nasal swabs, throat swabs, nasal aspirate, nasal washes, NP wash, and NP aspirate. For patients hospitalized with pneumonia, specimens from the lower respiratory tract

should also be obtained. Lower respiratory tract samples suitable for RT-PCR include: bronchoalveolar lavage, bronchial wash, tracheal aspirate, and lung tissue.

- Swab specimens should be collected using swabs with a synthetic tip (e.g., polyester or Dacron®) and an aluminum or plastic shaft. Swabs with cotton tips and wooden shafts are NOT recommended. Specimens collected with swabs made of calcium alginate are NOT acceptable.
- Place appropriate swab specimen in a standard container with 2–3 ml of viral transport media (VTM).
- Specimens should be collected within the first 24–72 hours of onset of symptoms and no later than 5 days after onset of symptoms. The specimens should be kept refrigerated at 4°C and sent on cold packs if they can be received by the laboratory within 3 days of the date collected. If samples cannot be received by the laboratory within 3 days, they should be frozen at -70°C or below and shipped on dry ice. The CDPH-VRDL is able to receive specimens Monday through Friday.

Recommendations for RLN laboratories

- During the 2016–2017 influenza season, RLN laboratories are advised to continue broadened surveillance testing for all influenza viruses in persons with:
 - ILI, especially for ICU and fatal cases
 - Outbreaks of acute respiratory illness
 - Cases where history of travel or recent close contacts or exposures within 10 days of symptom onset suggests concern for variant or novel influenza infection (e.g., swine (H3N2v) influenza, influenza A/H7, influenza A/H5, or other novel influenza A), as indicated above.
 - CDPH and CDC recommend testing of all hospitalized cases with ILI, as resources permit and at the discretion of the LHJ.
- To detect novel and possible reassorted viruses, it is important that laboratories use a full real-time RT-PCR subtyping panel (Inf A, H3, pdm Inf A, and pdm H1) to determine subtype. Typical Seasonal Influenza testing results are shown below:

Influenza real-time RT-PCR results for seasonal influenza viruses				
Influenza real-time RT-PCR Targets:	Inf A	H3	pdm Inf A	pdm H1
A/H1 2009 pdm virus*	POS	NEG	POS	POS
A/H3 seasonal virus	POS	POS	NEG	NEG

* Influenza A(H1N1)pdm09 virus

- Specimens with real-time RT-PCR test results that are inconclusive or meet any of the following criteria should be reported and submitted to CDPH-VRDL for further characterization as soon as possible (contact **Hugo Guevara at 510-248-9855**):
 - **Unsubtypeable** results with cycle threshold (Ct) value for Flu A ≤ 35
 - Inconclusive results for Influenza A(H1N1)pdm09 virus with Flu A Ct ≤ 35
 - Specimens with results suggesting the presence of more than one influenza virus (co-infections)
 - Specimens with results suggestive of variant (swine origin) influenza:

Influenza real-time RT-PCR results suggestive of variant (swine origin) influenza virus				
Influenza real-time RT-PCR Targets:	Inf A	H3	pdm Inf A	pdm H1
A/H3 variant virus	POS	POS	POS	NEG
Other A variant virus	POS	NEG	POS	NEG

- RLN laboratories should refer to the [Influenza Reference Examination Form](#) and the [VRDL General Submittal Form](#) for instructions on submission of specimens for further characterization at CDPH-VRDL.
- For influenza NEGATIVE severe or fatal ILI cases and for respiratory outbreak cases, VRDL will accept specimens for further non-influenza respiratory virus testing . Please use these 2 forms: [Non-Influenza testing form](#) and the [VRDL General Submittal Form](#).
- Each week please email influenza test results to CDPH at InfluenzaSurveillance@cdph.ca.gov. A template worksheet will be distributed to all RLN labs in a separate email prior to the start of the influenza season. If possible, please note if test results originate from outpatient, hospitalized, ICU or fatal cases.
- For fatal cases, refer available autopsy tissues to CDPH-VRDL for further testing and histopathologic analysis at CDC. For consultation on these cases, please contact **Hugo Guevara at 510-248-9855**.
- On a case-by-case basis, refer clinical specimens for antiviral resistance testing to CDPH-VRDL (e.g., a patient on treatment with persistently positive influenza PCR results). For consultation on these cases, please contact **Hugo Guevara at 510-248-9855**.
- Submit surveillance samples to CDPH-VRDL for strain-typing and antiviral viral resistance (AVR) according to the Influenza RightSize Roadmap sample targets for your LHJ. The sample sizes will be distributed to all RLN labs in a separate email.

- For local public health laboratories serving health jurisdictions with populations <750,000 residents, CDPH requests the submission of a minimum of one of each type/subtype laboratory-confirmed influenza positive specimens to CDPH-VRDL as follows:
 - At the beginning of the influenza season*
 - During the peak of the influenza season
 - At the end of the influenza season

***At beginning of the season:** Do NOT batch-send your samples, instead please submit specimens as they are detected by your laboratory.
- Submit original clinical specimens; if virus has been cultured, also submit the cultured virus. For more information contact **Hugo Guevara at 510-248-9855**.

Testing performed at CDPH-VRDL

- Testing at CDPH-VRDL will include outpatient ILI specimens submitted by sentinel providers and reference/confirmatory testing as requested by local public health laboratories.
- CDPH-VRDL and CDC will perform surveillance testing for strain-typing and antiviral resistance on the majority of specimens submitted that have been subtyped by RLN laboratories.
- Questions regarding respiratory virus testing at CDPH-VRDL can be directed to **Hugo Guevara** [*Hugo.Guevara@cdph.ca.gov* or 510-307-8565 or 510-248-9855 (cell)].

III. Reporting of severe influenza cases

- During the 2016–2017 influenza season, LHJs should continue mandatory reporting of laboratory-confirmed influenza in fatal cases aged 0–64 years.
 - Once the resolution status of an influenza death is set as “confirmed” in CalREDIE, it will be included in the state weekly report, and pediatric deaths will be reported as confirmed to CDC.
 - If you plan on issuing a press release regarding your jurisdiction’s influenza death(s), please ensure the case(s) has been reported to the CDPH influenza staff (i.e., “confirmed” in CalREDIE or paper case report form has been faxed) and also notify the State Press Office (**Office of Public Affairs, 916-440-7259**) prior to the press release.
 - The resolution status should be set to “confirmed” in CalREDIE once the death meets the case definition. If fatal cases reported by your county meeting the case definition have a “suspect” status, please confirm them as soon as your investigation permits. This will help us minimize the lag in reporting of fatal cases and allow our official counts in the state weekly report to be consistent with what is also being reported by LHJs.

- LHJs are strongly encouraged to continue voluntary reporting of laboratory-confirmed influenza cases aged 0–64 years requiring intensive care.
 - Once the resolution status of an influenza intensive care unit admission is set as “confirmed” in CalREDIE, it may be included in the state weekly report.
- LHJs should report fatal and ICU cases of laboratory-confirmed influenza to CDPH using CalREDIE or faxing the [Severe Influenza Case History Form](#) to 916-440-5984.

IV. **Mandatory reporting of fatal Respiratory Syncytial Virus cases** **NEW!!**

- During the 2016–2017 influenza season, LHJs should report laboratory-confirmed respiratory syncytial virus (RSV) in fatal cases aged 0–4 years.
 - Once the resolution status of an RSV death is set as “confirmed” in CalREDIE, it may be included in the state weekly report.
 - If you plan on issuing a press release regarding your jurisdiction’s RSV death(s), please ensure the case(s) has been reported to the CDPH influenza staff (i.e., “confirmed” in CalREDIE or paper case report form has been faxed) and also notify the State Press Office (**Office of Public Affairs, 916-440-7259**) prior to the press release.
 - The resolution status should be set to “confirmed” in CalREDIE once the death meets the case definition. If fatal cases reported by your county meeting the case definition have a “suspect” status, please confirm them as soon as your investigation permits. This will help us minimize the lag in reporting of fatal cases and allow our official counts in the state weekly report to be consistent with what is also being reported by LHJs.
- LHJs should report fatal cases of laboratory-confirmed RSV to CDPH using CalREDIE and either faxing the [Respiratory Syncytial Virus Death Form](#) to **916-440-5984** or uploading it to the electronic filing cabinet in CalREDIE.

V. **Reporting of non-TB respiratory outbreaks**

- CDPH also requests reporting of any acute respiratory outbreaks using CalREDIE or faxing the [Acute Respiratory Illness Outbreak Form](#) to **916-440-5984** in the following situations:
 - Outbreaks in institutions (e.g. long term care facilities, prisons, sleepover camps) with at least **one** case of laboratory confirmed influenza in the setting of a cluster (≥ 2 cases) of ILI within a 72-hour period.
 - Even if it is not influenza season, influenza testing should occur when any resident has signs and symptoms that could be due to influenza, and especially when two residents or more develop respiratory illness within 72 hours of each other.

- Outbreaks in institutions or congregate settings (e.g., schools, day camps) associated with hospitalizations or fatalities. If the setting is a hospice or long-term care facility, the LHJ should use its judgment as to whether the number of hospitalizations and/or fatalities is above baseline for that institution or setting.
 - Outbreaks in an institution, congregate setting or community where there has been recent exposure to swine for at least one case, or contact with a confirmed case of swine influenza (e.g., H3N2v).
 - Outbreaks in a community assessed by the LHJ as having public health importance.
- Laboratory confirmation can include any positive test performed by any clinical, commercial or local public health laboratory, including by positive rapid antigen test, direct fluorescence assay, culture or PCR.
 - Because influenza rapid antigen tests may yield a relatively high proportion of false positive results when influenza prevalence is low, it is recommended that a positive influenza rapid antigen test result be followed up with confirmatory testing using one of the other indicated methods. For cases of severe influenza, specimens should be sent for further subtyping/characterization to the local public health laboratory or CDPH-VRDL, to enable CDPH to closely monitor influenza viruses that may be novel or resistant to antiviral medications.
 - Outbreak reports may be completed by LHJs in CalREDIE or by submitting the hardcopy [Acute Respiratory Illness Outbreak Form](#) by email to CDOUTBREAK@cdph.ca.gov or fax to **916-440-5984**.
 - Once the resolution status of an outbreak is set as “confirmed” in CalREDIE, it may be included in the state weekly report.